NavMed 369

UNITED STATES NAVY

MEDICAL NEWS LETTER

Editor - Captain F. W. Farrar, MC, USN

Vol. 12 Friday, 27 August 1948 No. 5

TABLE OF CONTENTS

Circular Letters:

NOTICE

Because of easier reading and lower costs, the change to yellow paper is made for this and future issues.

The Diagnosis of Ionizing Radiation Injury by Physical Examination and Clinical Laboratory Procedures: The purpose of this report is to outline the available knowledge on the diagnosis of ionizing radiation injury by means of physical examination, and laboratory procedures. Dosimetry, the basis of prevention, will be referred to only for illustrative purposes.

Observations from animal experimentation are cited when data for human beings are lacking or are inadequate. It must be fully appreciated that the relationship between time of exposure and the appearance of signs and symptoms is not the same for man and smaller laboratory animals. All values for radiation dosage and laboratory procedures are the best possible estimate, based on available knowledge, and will have to be modified as more precise information becomes available.

Both acute and chronic effects may result from either internal or external ionizing radiation. The resulting clinical and laboratory picture is directly related to the amount of radiation, its rate of delivery, and the depth of dosage. This report deals with (1) the single intense exposure and (2) the repeated exposure of lesser intensity.

Diagnosis of single intense exposure to ionizing radiation. A single intense exposure is defined here, arbitrarily, as a total body exposure of more than 25 roentgen units delivered within a few hours. An exposure of 25 r is set as the lower limit because the effects of lesser amounts are most difficult, if not impossible, to detect by clinical means. Whether lesser amounts may produce deleterious late effects is not known with certainty. The effect of exposure to ionizing radiation is determined to a considerable extent by the physical characteristics of the ionizing radiation concerned, that is, the type (alpha, beta, gamma, x-ray, or neutron), the ability to penetrate (type and energy), and the rate at which the radiation is being delivered. With a single accidental exposure that may occur, these physical characteristics are usually known. Dosimetry determines to a large extent the above-mentioned physical characteristics. These physical characteristics are important because the clinical picture varies with the number of organ systems involved. Total body exposure to highly penetrating radiation, in which all organ systems are effected, produces a more severe picture than total body exposure to an equivalent amount of radiation absorbed superficially.

The symptoms in man following the single intense exposure are quite well known from the experiences of the Japanese following the atomic bomb explosions over Hiroshima and Nagasaki.

A few hours after exposure to the ionizing radiations of the atomic bomb, nausea and vomiting appeared. This lasted for a few hours and then subsided for a latent period of a varying number of days. The shorter the latent period the more severe the recurrent nausea and vomiting, mucous or bloody diarrhea, purpura, epilation, and agranulocytic infections. In general,

the tempo at which the disease progressed in the Japanese and the Bikini animals was directly related to the amount of radiation received.

The latent period, the length of time between exposure and the development of symptoms, is of great interest. The duration of this period in mammals is inversely proportional to the amount of radiation received. With very large amounts of radiation, in excess of 10,000 r, the latent period becomes very short and death may occur within 24 hours or even while the radiation is being received. Each species has its characteristic latent period for the development of all symptoms. In goats it appears to be from 3 to 5 days; in swine it is approximately from 5 to 7 days. In man it is probably longer. It is important to remember that with short latent periods death may occur before the full syndrome develops.

In the case of ionizing radiation that can penetrate only a few millimeters of tissue, signs, and symptoms are limited to the surface of the body. In general, it may be stated that the effects upon skin resemble thermal burns, and that anything from erythema and massive vesiculation to full thickness destruction of the skin may occur.

The early hematologic response of man to single intense exposures to ionizing radiation is not well known because the early blood changes were not observed in the Japanese. Reference will therefore have to be made to laboratory animals in order to get an idea of what might be expected. There is no reason to expect any qualitative difference in the response of man and animals, but there may be significant differences in sensitivity and rate changes in the peripheral blood. The hematologic responses of laboratory animals to single intense exposures to penetrating ionizing radiation are quite uniform. However, following exposure to less penetrating radiation the blood changes may be fleeting, slight, or absent despite severe superficial injury.

Beginning shortly after exposure to penetrating radiation there is a prompt decrease in the total lymphocyte count which is most marked within from 24 to 72 hours, depending upon the amount of radiation received. Recovery following a nonlethal dose begins within a few hours or days. Developing simultaneously with the progressive lymphocytopenia is a moderate granulocytic leukocytosis which appears as two peaks approximately 12 and 24 hours after exposure in rabbits. If counts are not performed at about hourly intervals one of the peaks may be missed. After the 24-hour peak there is a progressive decline in the count for granulocytes for the next 4, 5, or 6 days; then there is a fleeting increase in granulocytes which reflects a wave of bone marrow activity. This activity is short lived and the granulocytes again decrease. The subsequent course depends upon whether the exposure is lethal or nonlethal. About from 15 to 17 days after nonlethal exposures a sustained though small rise in the granulocytes appears. In lethal exposures this sustained return of granulocytes is absent. Granulocytic leukocytosis may not occur after very heavy radiation.

Reduction in the number of platelets, red cells, and the morphologic changes in the leukocytes appear more slowly and are not so uniformly observed. In the Bikini goats and swine a marked shower of immature red cells appeared in the peripheral blood from 10 to 12 days after the atomic bomb air burst. This phenomenon has been repeatedly observed in smaller laboratory animals. Atypical and immature leukocytes and nucleated red cells appear in the peripheral blood beginning from 3 to 10 days after exposure.

Concerning the single intense exposure to ionizing radiation it is believed that the following can tentatively be stated regarding man, until actual observations substantiate or refute these suppositions. If no decrease in the total lymphocyte count occurs in the first 48 hours, usually the first 24 hours, the exposure has certainly been less than 25 r and symptoms probably will not appear. If exposure has been between 25 and 100 r a fleeting lymphocytopenia will develop and symptoms will probably be mild. If exposure is between 100 and 200 r the lymphocytopenia will be of greater severity and last longer, and severe symptoms of radiation illness and death will occasionally occur. If exposure is greater than 200 r the symptoms of radiation illness will be much more severe and deaths will occur more frequently. The leukocytic changes, particularly the early lymphocytopenia, will be marked.

The determination of a decrease in total lymphocytes or total leukocytes unfortunately cannot be based on a normal average for man or animals. The range of normal blood cell counts is wide for all animals, including man. Normal hematologic values of man will be considered in the second part of this report along with schemes for the detection of deviation from the normal ranges. Needless to say, in order to detect fleeting changes in members of the leukocyte population total white and differential blood cell counts must be performed every hour or so.

Diagnosis of acute radiation illness by the leukocyte count is obviously totally impractical under conditions of a catastrophe or atomic warfare. Hence the development of an easily-read casualty dosimeter is imperative.

The diagnosis of cumulative small exposures to ionizing radiation. The diagnosis of repeated small exposures to ionizing radiation presents an entirely different problem. The changes are insidious and progressive. If excessive cumulative exposure is not detected early, serious or fatal changes may develop. At the present time 0.1 r per day has been set as the maximum amount of radiation that can be tolerated with impunity. Animal experimentation by Lorenz et al. on mice suggests that the tolerable dose of radiation for females should be set even lower because of a possible increased incidence of ovarian tumors.

The physical characteristics of the radiation determine to a great extent the effects that will appear from chronic exposure. The penetrating radiation may result in generalized systemic and hematologic disorders in addition to the purely superficial effects of radiation with a very low degree of penetrability.

The physical characteristics of the radiation are usually known as a specific job hazard. Relative exposure to beta, soft x-ray, and gamma radiation is determined by suitable dosimeters.

The superficial lesions that appear are largely limited to the skin and eyes. Cutaneous lesions are apt to appear in fluoroscopists, radiochemists, and radium handlers. An increased brittleness of the finger nails with a tendency to develop increased longitudinal ridges is common. Later there may be a loss of the integrity of the fingerprint due to patches of atrophy. Pigmentation, ulceration, and carcinoma may follow the atrophy. Epilation of hairy parts may occur. Impaired sensation of the finger tips commonly accompanies the above changes. In the eyes, radiation cataracts may occur at an early age. However, the alteration in the blood is the best biological index of chronic total body overexposure to ionizing radiation.

Many investigators have called attention to the great variations of the blood responses of man chronically exposed to ionizing radiations. Leukocytosis, lymphocytosis, leukemoid reactions, leukocytic leukemias, erythrocytosis, reticulocytosis, leukopenia, thrombopenic purpura, aplastic anemia, and leukopenic leukemias have all been reported as produced by chronic exposure to radiation. The blood picture may be temporarily or permanently altered by many diseases and industrial intoxications in addition to radiation. For example, infectious mononucleosis may affect the total and differential white blood count of young adults for many months after symptomatic recovery. Examples of industrial poisons which affect the blood are benzol and heavy metals. Hence it is apparent that a "normal" range of blood counts for man must be established. This is difficult because the blood picture varies with age and to a varying degree with sex, pregnancy, meals, humidity, and temperature.

In naval personnel between the ages of from 17 to 35, without any recent history or sign of disease, the total white cell count varied from 4,000 to 16,000 in the tropics and in a temperate zone. The total lymphocyte count was usually below 3,000 and rarely above 5,000. Probably 90 percent of the adult population will have total white counts between 5,000 and 11,000 per cmm. The 10 percent of adults whose counts are outside of this range may cause considerable consternation in a radiological safety program and lead to medicolegal problems.

Goldwater has correctly called attention to the wide range of normal lymphocyte counts in his data and in that of Osgood. The data on naval personnel are similar. In addition, Goldwater calls attention to the necessity of having comparable parallel control studies on persons that are not subjected to any known toxic agents.

Because the average count is not dependable for the general population or specific age groups, base line complete blood counts must be performed on all individuals before exposure takes place. Subsequent counts should be performed at not less than monthly intervals. Notations on the occurrence of colds and infections must parallel the blood records, for without these base line records

and a knowledge of each individual's response to infections, an evaluation of leukocyte changes is more difficult.

A partial review of the literature confirms the opinion that the presence of any of the following alterations in a person whose usual blood values are known and who has been exposed to ionizing radiation constitutes presumptive evidence of excessive exposure until proved otherwise:

a. A persistent depression of the total leukocyte count below 4,000 per cmm.

b. A persistent elevation of the total leukocyte count above 15,000 per cmm. with an absolute lymphocytosis.

c. A relative lymphocytosis with a low total count (from 4,000 to 6,000 per cmm.) that returns to base line range following removal from exposure.

d. A macrocytosis.

e. A reticulocyte count over 2 percent.

f. An erythrocytosis:
   (1) Red blood cell count over 5.8 million per cmm.
   (2) Hemoglobin over 18.0 Gm. per 100 c.c. blood.

Many other phenomena have been suggested as hematologic evidences of excessive exposure. Changes in blood coagulation, prothrombin time, platelets, and morphologic changes in leukocytes have been suggested. It is exceedingly difficult to evaluate the importance and the diagnostic value of these changes. A more recent observation on excessive exposure concerns refractile bodies ("Dickie bodies") in the lymphocytes (See Medical News Letter of 24 October 1947.). These refractile bodies are stained with neutral red in a supravital preparation. It has been reported that increased numbers of these bodies are specific evidence of exposure to radiation or industrial poisons. The procedure for detecting the presence of Dickie bodies necessitates a flawless supravital technic which is not widely available, hence the technic may not be generally useful.

The foregoing criteria depend upon abnormalities in the numbers or structure of blood cells which arise from either depressed hematopoiesis, an increased lability of the hematopoietic organs, or abnormal maturation. The determination in exposed persons of the presence of these criteria can be attained by establishing a comparable control group the members of which are not subjected to any known toxic agent. Average values for exposed and control groups should be studied statistically to determine if there are significant differences between the means of the two groups. In a comparable fashion the pre-exposure counts of the exposed group can be used as the control. If the average leukocyte count of the group for a given exposure period is significantly less

than the average leukocyte count of the group of the pre-exposure period, it can be stated with considerable certainty that excessive exposure to ionizing radiation or other toxic agent has occurred.

The following procedures will aid in determining the cause of any abnormal blood findings in a person suspected of having been excessively exposed:

a. Remove the suspect from all possible exposure to ionizing radiation.

b. Make differential counts of radiation on excreta, nasal swabs, and expired air in order to estimate the type and degree of internal exposure to radioactive isotopes.

c. Study the blood at weekly intervals and compare with the pre-exposure base line leukocyte counts and search for an increase in the number of highly refractile neutral red bodies in the lymphocytes.

d. Endeavor to eliminate other factors such as infectious lymphocytosis, infectious mononucleosis, virus disease, benzol poisoning, and heavy metal poisoning.

Summary and Conclusions. The diagnosis of a single excessive exposure to ionizing radiation by blood examination is not difficult. If serious exposure has occurred, a prompt, marked lymphocytopenia results and is followed by a characteristic sequence of events in the other members of the leukocyte population.

The diagnosis of repeated exposures to small amounts of ionizing radiation in an individual is difficult and uncertain. It requires in addition to blood studies, differential counts of radiation in urine, feces, and nasal secretions, and, the elimination of other industrial hazards.

The determination of repeated exposure to small amounts of ionizing radiation in personnel groups by the statistical comparison with a control group or by statistical comparison of the pre- and post-exposure average leukocyte count is a reasonably accurate diagnostic procedure.

The main bulwark of protection from ionizing radiation must remain physical control of radiation intensities by established monitoring procedures and prevention of contamination of personnel by radioactive materials. This is essential because most of the signs and symptoms appear relatively late after the radiation injury has been sustained. (Proj. NM 007 039, Rep. No. 8, 8 April '48, Nav. Med. Res. Inst., Bethesda, Md. - E. P. Cronkite)

* * * * * *

Study on Acquired Resistance of Flies to DDT: Because it was indicated in numerous reports that less effective control of flies was occurring in buildings

where DDT residues have been employed for several years, a study of the comparison of flies collected from untreated and DDT-treated areas was undertaken by Gahan et al. of the laboratory of the Bureau of Entomology and Plant Quarantine, U. S. Department of Agriculture, at Orlando Florida.

About from 200 to 400 flies were collected from each of 4 dairies that have been using residual DDT control for at least 3 years, and from 2 hog pens, a horse stable, and a city dump where DDT residues have not been used. Eggs were collected at 2-day intervals until three sets had been obtained from each group. Eight colonies of flies, each consisting of 3 batches, were reared from them. All insects received identical care. Tests were run with these flies in comparison with 2 lots from the regular colony maintained at the laboratory to determine their relative resistance to DDT residues. For these tests 10 cloth panels were treated at the rate of 100 mg. of DDT per square foot. The flies were confined on the panels under petri dishes for 10 minutes, after which they were held in clean holding cages until the 24-hour mortality counts were made. To compensate for any difference in treatment, the panels were rotated after each test and exposures on four panels were made with each batch of flies. One batch of flies from the Eunice dairy and one from the pig pen in Forest City escaped from the holding cages before they could be used, so these tests were replicated only twice.

The lowest average mortality occurred among the flies collected in the treated dairies. However, there was considerable variation between the different places, and one colony from an untreated dump showed lower mortality than 3 of the 4 colonies from the treated dairies. The average differences were too small to indicate a significant difference in susceptibility. The average mortality for the flies from the laboratory control colony was somewhat higher than that for either of the other groups. (Second Quarterly Research Progress Rep., 1948, Bureau Entomology and Plant Quarantine, U. S. Dept. Agriculture)

* * * * * *

Sinusitis in Children: Many adults suffering with chronic inflammation of the nasal accessory sinuses give a definite history of nasal infection in infancy and early childhood. Many of the complications of sinusitis are of a serious nature to the child and cause morbidity in adult life. Ebbs made a routine survey of the nasal sinuses at autopsy in 495 children up to the age of 14 in whom the cause of death was not related to sinusitis. In 152 (30.6 percent) he found that one or more of the nasal sinuses contained free pus.

The frontal sinus is not present at birth. It assumes importance in childhood at about the eighth year. The maxillary sinus is present at birth and is of clinical significance at all ages. The ethmoidal sinuses develop early and are of importance in childhood. The sphenoid is of very little significance in childhood.

Allergy is a common etiologic factor in children. Other causitive factors are the common cold, anatomical abnormalities, tonsils and adenoids, swimming, endocrine disorders, and poor hygienic conditions.

The nasal mucosa in childhood is more prone to infection than it is in adults. The diagnosis is based upon the history, examination, and x-ray findings.

In the examination of the nose one must note the color of the mucous membrane; if unusually pale and edematous, allergy is suggested. Unilateral purulent discharge is usually due to one of three conditions: sinusitis, foreign body or diphtheria. The author believes that it is a good routine procedure to spray the nose with ephedrine or an ephedrine-like drug. Often pus can be seen in the nose after shrinking when it could not have been demonstrated otherwise. If necessary, the nose can be desensitized by either packing with a 5-percent solution of cocain, or spraying with a 2-percent solution of pontacain. The nasopharygoscope can be used in older children. Transillumination is important for the maxillary sinus, but it is of questionable value in the diagnosis of frontal sinusitis. Even in maxillary involvement the author has found the sinus clear to transillumination and then has washed out considerable pus. X-ray examination is of definite value, especially if the sinuses are clear. However, if the sinuses show an equal degree of mild cloudiness, it is often impossible to differentiate between sinusitis and allergy. Radio opaque materials may be injected into the maxillary sinuses or instilled by the displacement method. No trouble has been found in using the Proetz method for this purpose, but it is rarely necessary in children.

Differential diagnosis from allergy is most important and most difficult. Rawlins lists the following as suggestive of allergy:

Stuffy nose; postnasal, and at times, anterior nasal discharge which is usually mucoid and usually worse in the morning; dull generalized headache with inability to concentrate; nasal surgery without permanent relief; sneezing; itching of the nose, eyes, and throat; chronic cough; ear symptoms (Allergic catarrhal middle ear symptoms are fairly common in children.); frequent colds (often allergic flare-ups); adenoid type of mouth breathing; fatigue; chronic hoarseness; sore throat; improvement of symptoms in dry atmosphere; flareups from emotional stress; symptoms perennial but often worse in winter; the presence of environmental factors both at home and at work which could cause allergic rhinitis; the presence of asthma, hay fever, eczema, uticaria, and indigestion after eating certain foods; family history of an allergic condition.

In a patient with a typical case of allergy, the mucous membranes of the nose are pale and edematous. The nose and postnasal space is often filled with thick mucus. A smear from this mucus should be examined for cells. If eosinophiles are found in abundance allergy is strongly suggested. The best method is to have the patient blow his nose on waxed paper and examine the mucus. A postnasal or nasal smear may aid. Many rhinologists use a light suction for removing the mucus both postnasally and anteriorly. If these methods fail the author resorts to a Proetz displacement instillation with sterile normal saline. The washings

are centrifuged and the residue examined for eosinophiles. A culture is also made by this method. The author and co-workers obtain mucus not only from any hidden recesses but from the sinuses themselves. Ashley does not believe that it is possible to diagnose a condition as one of allergy unless eosinophiles are found. However, the author believes that a diagnosis can often be made from the history and findings alone, even if eosinophiles are not found. Many patients in whom eosinophiles were never found, have been proven allergic by their positive reactions to intradermal tests and their subsequent relief following treatment for the allergy.

The treatment of acute sinusitis in children consists of bed rest, sulfa drugs, x-ray therapy, penicillin, and surgery rarely (only in cases in which grave complications threaten).

The treatment of chronic sinusitis consists of management of the allergy; irrigation of the maxillary sinus; Proetz displacement treatments; regulation of diet; correction of endocrine disorders; surgery, when conservative measures fail to give satisfactory results.

The complications consist of eye disorders, osteomyelitis, meningitis, pulmonary diseases, arthritis, and ear diseases. (Arch. Pediat., June '48 - L. K. Gundrum)

* * * * * *

Plasma in the Treatment of Post-Measles Encephalitis: The author states that during the past 26 years he has observed many fatal cases of post-measles encephalitis. The last 4 patients, however, with plasma therapy, all recovered.

Case Reports Case 1. Male, age 7. After 3 days of increasing symptoms the rash first appeared on 28 June 1947. On 30 June the temperature was normal. On 1 July at 5:00 A.M., the child became stuporous and remained so for 4 days at home, the temperature reaching 105.4° F. before hospital admission. The spinal fluid cell count totaled 550, of which 320 were white blood cells, 86 percent lymphocytes and 14 percent polymorphonuclears. The total protein was 132 mgms. percent, the sugar 46 mgms. percent, the smear and culture, negative. The temperature ranged from 102° to 105.6° F. the first day; from 99° to 102.2° F. the second day; and from 99° to 101.8° F. the third day. It remained normal on the fourth day.

Plasma, 500 c.c., was given every 12 hours during the first two days and 500 c.c. on the third day - a total of 2,500 c.c. On the first day, 500 c.c. of 5-percent glucose in normal saline was also given.

The day following admission, the child was much less stuporous and definitely improved. On the fourth day the child appeared almost normal. He was discharged from the hospital on 19 July 1947.

Case 2. Male, age 26. Rash first appeared 25 April 1947. Drowsiness was followed by stupor on 28 April 1947 when the patient was admitted to the hospital with a temperature of 105.4° F. The spinal fluid revealed a total cell count of 138, 50-percent lymphocytes and 50-percent polymorphonuclears; Pandy's test 1+. Plasma 1,000 c.c. was given for the first two days and 500 c.c. on the third day. The response was definite within 24 hours, with the temperature normal on 2 May. Spinal fluid on 5 May 1947 revealed 17 cells. The white blood cells were 11,000 on admission and 7,950 on 10 May.

He was discharged from the hospital on 12 May 1947.

Case 3. Female, age 8. Rash first appeared on 2 May 1947. On 5 May 1947 the patient became stuporous. She was admitted to the hospital on 6 May 1947 with a temperature of 102° F. The spinal fluid cell count was 66 cells, 60-percent lymphocytes and 40-percent polymorphonuclears. Pandy's test showed 2+, total protein 92-mgms. percent and sugar 58-mgms. percent. Plasma, 500 c.c., was given intravenously every 12 hours for 5 doses. On 7 May, 24 hours after admission, she was entirely free of stupor and her temperature was normal on 8 May. She was discharged on 12 May 1947.

Case 4. Female, age 8. Rash first appeared on 18 June 1947. She was admitted to the hospital 23 June 1947 with severe convulsions which continued for two hours. Upon admission the child was quite cyanotic, and her pulse was weak. It was believed that she was "in extremis." Her admission temperature was 102.4° F. Oxygen and plasma were started at once; mucus was suctioned when necessary.

The spinal fluid showed a cell count of 28, of which 11 were white cells, 10 lymphocytes. Pandy's test was 2+. The total protein was 72-mgms. percent; sugar 76.3-mgms. percent. Her convulsions ceased after she received 200 c.c. of plasma. Stupor subsided entirely within 36 hours, and her temperature remained normal after 48 hours. The total amount of plasma received was 500 c.c. every 12 hours for 5 doses. She was discharged on 27 June 1947.

In all patients, if the plasma seemed insufficient, adequate fluids were administered, either by venoclysis or by mouth as soon as the patient responded. There were slight reactions from the plasma which were believed to have been caused by the rubber tubing.

In this small group of patients, the effect of plasma seemed dramatic. It is possible that the plasma supplied some of the electrolytic needs of the involved cerebral cells as well as measles antibodies. Assuming that this premise could be true, the earlier the diagnosis is established and the treatment begun, the sooner the response will be and the sequelae lessened. (Arch. Pediat., June '48 - C. L. Thenebe)

* * * * * *

A Study Concerning Vitamin K_5: This report deals with new biological observations on one of the vitamin K analogues, vitamin K_5, known chemically as 2-methyl-4-amino-1-naphthol hydrochloride. This compound which has been used with remarkable success as a water-soluble form of antihemorrhagic vitamin, is characterized by low toxicity for animals, the LD_{50} for mice being approximately 750 mg. per Kg. when administered orally or intraperitoneally. Due to their inhibitory action on the formation of acid in saliva, both vitamins, K_3 (2-methyl-1, 4-naphthoquinone) and K_5, may find practical application in the prevention of dental caries. Vitamin K_3 and 2-methyl-1,4-naphthohydroquinone retard the growth of Penicillium notatum, of other fungi, and of yeasts. It appears that vitamin K_5 has not been studied for such properties.

In this study, it was found that vitamin K_5 at a concentration of 0.1 Gm. per L. prevents growth of Penicillium notatum NRRL 1249.B4 on a rich culture medium. Growth of Trichophyton mentagrophytes was prevented by K_5 at a concentration of 10 Gm. per L. in agar cup-plate tests or by 0.01 Gm. per L. when the compound was incorporated in the nutrient substratum. The compound is strongly antagonistic also to Microsporum canis, Microsporum audouini, and Botrytis allii. Concentrations of 25 mg. or more of K_5 per L. checked fermentation by yeast (Saccharomyces cerevisiae) in a 10-percent glucose solution.

The experimental results with vitamin K_5 are in accord with those of Ball et al., who found that substituted naphthoquinones prevent the oxidation of p-phenylenediamine and interfere with the respiratory systems at a redox potential between those at which cytochrome C and cytochrome B operate. More specifically vitamin K_5 may be assumed to interfere with the component which Bach et al., consider necessary for the reduction of cytochrome C by cytochrome B, and which Slater tentatively identified as a haematin compound. It may be suggested that vitamin K_5 may act by the same mechanism that Schonberg and coworkers postulated for the various naphthoquinones, viz., by virtue of a high oxidation-reduction potential.

Because of its fungistatic activity and its low toxicity, vitamin K_5 may prove of value for the preservation of foods and beverages as well as for the clinical treatment of infections with dermatophytic fungi. (Proc. Nat. Acad. Sc., July '48 - R. Pratt et al.)

* * * * * *

Vitamin B_{12} - A Cobalt Complex: The following observations have been made on vitamin B_{12}, previously described by the authors (Medical News Letter, 7 May 1948) as a red crystalline compound, which is highly active for producing hematological responses in patients with pernicious and other anemias, and for the growth of Lactobacillus lactis, chicks, and rats.

Spectrographic analysis of B_{12} has shown the presence of cobalt. This vitamin appears to be a cobalt coordination complex which, having 6 groups about the

cobalt atom, could involve one or more organic moieties. The red color of B_{12} appears to be at least in part associated with its cobalt-complex character.

The presence of cobalt reflects significantly upon many biological studies which have shown that cobalt is an essential trace element in nutrition, and perhaps upon suggestions concerning cobalt as a trace contaminant in iron therapy of anemias. The nutritional significance of cobalt must be re-evaluated as the biological function of B_{12} is developed.

Cobaltous ion (1 ug. per ml.) was without activity for L. lactis as contrasted with the high potency of B_{12} (0.000013 ug. per ml., half-maximal growth).

Randolph West has tested cobalt ion in two cases of pernicious anemia with negative results. The average adult daily dietary intake of cobalt has been estimated at 100 ug.

Spectrographic examination of B_{12} also showed the presence of phosphorus. Although nitrogen was found to be present, tests for sulfur were negative.

Microbiological assay of an aqueous solution of B_{12} (74 ug. per 0.5 ml.) showed that autoclaving for 15 minutes at 121° C. did not change its activity significantly.

Vitamin B_{12} in 0.015 N sodium hydroxide solution (0.2 ug. per ml.) was inactivated at room temperature as follows: 20 percent (0.67 hr), 45 percent (6 hrs), 90 percent (23 hrs), 95 percent (95 hrs); it was inactivated in 0.01 N hydrochloric acid solution (10 ug. per ml.) as follows: 18 percent (3 hrs), 75 percent (23 hrs), 89 percent (95 hrs).

The cobalt-complex nature of vitamin B_{12} is an outstanding property. (Science, 6 Aug. '48 - E. L. Rickes et al.)

* * * * * *

Fulminating Meningococcic Infections and the So-Called Waterhouse-Friderichsen Syndrome: Whenever the incidence of Neisseria meningitidis infections approaches epidemic proportions there is an increase in the fulminating fatal infections, frequently with few or no signs of meningeal involvement. The progress of the disease in these cases is so rapid that death commonly occurs within from 12 to 24 hours after the appearance of the first symptom. The presenting clinical picture is frequently one of pharyngitis, fever, and sometimes gastro-intestinal symptoms, followed by the rapid development of widespread petechiae, cyanosis, peripheral vascular collapse, and death. This condition has come to be known as the Waterhouse-Friderichsen syndrome, with collapse and sudden death supposedly produced as the result of massive bilateral hemorrhage into the adrenal glands. This syndrome occasionally has been reported as occurring in other types of fulminating bacteriemia, but most frequently is associated with N. meningitidis infections.

In the past few years the authors have had the opportunity of studying 16 cases of acute fulminating meningococcic infection at autopsy. N. meningitidis was recovered from cultures of either blood or cerebrospinal fluid, or both, in each case. The pathologic changes found at autopsy in these cases support the view that the presenting clinical syndrome is the result of an overwhelming bacteriemia and toxemia. It is an accepted fact that massive bilateral adrenal hemorrhage occurs in some cases, but from this series it would appear that these are only associated lesions and are not responsible in themselves for the clinical picture presented. Cases having the same clinical syndrome show no great destruction of adrenal cortical substance.

Five of the 16 case reports presented by the authors follow:

Case 3. A male, 20 years of age, was first seen about 4 p.m., complaining of sore throat. Examination was negative except for evidence of a marked pharyngitis. The patient was seen in the hospital at about 9 p.m. Temperature at this time was 102.5° F. and there were noted a very red throat and a few scattered petechiae in the skin. There were no neurologic signs but, because of the petechiae, a blood culture was taken and a lumbar puncture done. The cerebrospinal fluid showed 130 cells, mostly polymorphonuclear leukocytes. Four grams of sulfadiazine were given by mouth. The patient rapidly became disoriented and the petechiae increased. About 2 a.m., 10 hours after he was first seen, the patient developed respiratory failure and died. Autopsy revealed purpura in the skin and mucous membranes; bilateral massive hemorrhage in the adrenals; acute tracheobronchitis; and very early meningitis. Cultures of blood and cerebrospinal fluid were positive for N. meningitidis.

Case 4. A female, 30 years old, had felt well until afternoon of the day of onset, at which time she complained of a slight sore throat. During the evening she had noticed numbness and pain in the arms and legs. There had been no headache. She was seen by a physician at about 10:30 p.m., when her temperature was 100.4° F.; pulse rate, 96; respiratory rate, 20. Physical examination revealed a few petechiae in the skin. There were no positive neurologic findings. The petechiae rapidly became more numerous. The patient became drowsy and died about 4 a.m., approximately 12 hours from the onset. The autopsy showed purpura in the skin and mucous membranes; bilateral hemorrhages in the adrenals; and toxic changes in the spleen and kidneys. Cultures from the blood and cerebrospinal fluid were positive for N. meningitidis.

Case 8. A male, 44 years old, was admitted to the hospital in coma. There was an indefinite history of an upper respiratory infection. Otherwise he had been well until the morning of admission. At that time he became sulky and irritable, and later in the day, drowsy and incontinent of urine and feces. He was thought to be intoxicated. At 6 p.m., he was seen by a physician who noted petechiae on the body, and, nuchal rigidity. He was admitted to the hospital at 9 p.m. His temperature was 103° F.; pulse, 104; respiratory rate, 30; blood pressure, 80/40 mm. Hg. There were generalized petechiae and rigidity of the neck. Physical examination was otherwise negative. Lumbar puncture revealed 3,840 cells per cmm. There were many Gram-negative, intracellular diplococci. Cultures of the blood and cerebrospinal fluid revealed N. meningitidis. Intravenous sodium sulfadiazine was given, the patient receiving 7.5 Gm. in 6 and 1/2 hours. He became very restless, the pulse was rapid and irregular, and death occurred 8 hours after admission and approximately 22 hours from the onset of the illness. The autopsy disclosed purpura of skin and mucous membranes; moderate meningitis; and toxic changes in the spleen, liver, and kidneys.

Case 10. A female, 26 years of age, had had symptoms of a mild cold for 3 days. On the afternoon of admission to the hospital there had developed fever, vomiting, chills, and stupor, followed by convulsions. On admission the patient was stuporous. Petechiae had developed over the entire body. The temperature was 102° F.; pulse, 100; respiratory rate, 46; blood pressure, 140/60 mm. Hg. There was nuchal rigidity and a bilateral Babinski sign. The cerebrospinal fluid was slightly cloudy and contained pus cells and Gram-negative intracellular diplococci resembling N. meningitidis. Examination of the blood showed 8,400 white cells, with polymorphonuclear cells, 80 percent, and nonprotein nitrogen, 50 mg. percent. Blood culture was later reported as positive for N. meningitidis. Sodium sulfadiazine was given intravenously and a blood level of 14-mg. percent established. The patient was given also antimeningococcic serum, adrenal cortical extract intravenously, and parenteral fluid because of low urinary output. Twenty-four hours after admission she became irrational and died. Autopsy showed petechiae of skin and mucous membranes, toxic changes in kidneys, a few small hemorrhages in the adrenals, and cirrhosis of the liver. Post-mortem cultures of blood and cerebrospinal fluid were negative.

Case 15. A male, 1 year old, had had a mild upper respiratory infection for 2 days. Approximately 24 hours before admission the child was noted to be restless. This was followed in a few hours by vomiting and a red rash on the skin. The child was sent to the hospital. The temperature was 103° F.; pulse, 165, weak and rapid; respiratory rate, 65; blood pressure, 145/100 mm. Hg. The pharynx was red. There was nuchal rigidity, hyperactive reflexes, and bilaterally positive Kernig's sign. Lumbar puncture showed increased spinal fluid pressure, a cell count of 3600 per cmm. with 60 percent polymorphonuclear leukocytes and 40 percent lymphocytes, and chlorides, 680 mg. per 100 c.c. Meningococci were found in the fluid. The peripheral blood was not remarkable. The child was treated with penicillin intravenously and intrathecally and given sulfamerazine by mouth. Six hours after admission he was lethargic and semistuporous. Temperature was 104° F.; pulse, 175; respiratory rate, 85; blood pressure, 90/60. There were increasing numbers of petechiae and extreme cyanosis. Death occurred 8 hours after admission. The autopsy revealed petechiae over the upper body, a few petechiae in the serous membranes; blood-stained fluid in the left pleural cavity; congestion and edema of lungs; congestion of kidneys; negative adrenals; and meningitis.

In the 16 cases of overwhelming meningococcic infection presented, there was considerable variation in both the clinical syndrome and in the postmortem findings.

Of the 16 cases, 10 were in males and 6 were in females. The age varied from 3 months to 53 years. Nine were in children, ranging in age from 3 months to 8 years, and 7 were in adults from 20 to 53 years of age. Although the picture of overwhelming meningococcemia is one which is recognized by pediatricians, the rather common occurrence of this same condition in adults has not been generally recognized. Moritz and Zamcheck stated: "The incidence of rapidly fatal meningococcemia appears to be considerably higher in younger than in older soldiers." One of the most striking features of the disease is the rapidity of its progress. Although several of these patients had complained of an ordinary upper respiratory infection for a period of 2 or 3 days, most of them (or their parents) could place the onset of acute illness at some particular hour of the day or night. Within 24 hours death occurred in 12 of the 16, 3 survived for about 30 hours, and one survived for approximately 60 hours. Although the presenting symptoms varied considerably, it was notable that in adults pharyngitis was a common chief complaint, whereas in children, fever, headache, and irritability appeared to be particularly common. In patients who were seen by physicians, cyanosis was marked.

Purpura of the skin and mucous membranes was prominent in all patients except one. These hemorrhagic manifestations developed rapidly and could be seen to increase rapidly while the patient was under observation. Increasing cyanosis, delirium, stupor, circulatory collapse with falling blood pressure and death soon followed. Cases of this type have been known as the Waterhouse-Friderichsen syndrome. Martland found only 107 such cases prior to 1943 and added 19. Many have been described since.

In most cases the causative organism has been a meningococcus, but the Diplococcus pneumoniae, the Streptococcus haemolyticus (beta), the Haemophilus influenzae, and others have been reported. In all of the patients in this series the meningococcus was isolated from either the blood or cerebrospinal fluid, or both. This is in contrast with the statement of Rucks and Hobson that "search for the causative agent in the spinal fluid is generally fruitless." The reports of

McLean and Caffey and others, and more recently of Tompkins, on the recovery of organisms from the purpuric lesions, offer another method for the rapid recognition of the inciting factor.

At autopsy the striking change seen, in addition to those in the meninges and adrenals, is the microscopic evidence of diffuse and marked vascular damage with thrombosis, in many organs of the body. Thrombi were found in the capillary systems of various organs in all except one case - in the patient who survived for 60 hours. In the more severe areas of involvement almost every vessel, in some organs, was occluded by such masses of hyaline material. Such changes were seen in the heart, lungs, liver, kidneys, adrenals, pancreas, and gastro-intestinal tract, in varying degrees. Hill and Kinney have recently described the marked vascular damage and thrombosis which they found in the skin, membranes, and organs. In the present series there was no correlation between the amount or degree of thrombosis in one organ and in another, or between the occurrence of such thrombosis and the presence of meningitis. Extensive thrombosis was found in the organs of some patients in whom changes in the adrenal glands were comparatively slight. In others, massive thrombosis occurred in the kidneys and adrenals, and other organs showed comparatively slight changes. In 7 of these cases there was no gross hemorrhage into the adrenals and in 3 it was from slight to moderate. Even in cases in which it was marked, much surviving adrenal cortical tissue was seen when the glands were examined microscopically. In those cases in which the blood pressure was taken there was no correlation between the degree of adrenal cortical destruction and the level of the blood pressure. In those cases in which it was not taken, circulatory collapse was evident. Clinically, and otherwise at autopsy, the cases with and without massive hemorrhage into the adrenals cannot be separated. Boger stated: "Clinically, the term 'fulminating meningococcemia' seems preferable to 'Waterhouse-Friderichsen syndrome,' and if the latter has any usefulness it should be restricted to pathological discussions." From these studies its use does not appear to be justified even in pathologic discussions. There is evidence of an intense overwhelming bacterial infection with marked vascular damage resulting in thrombosis, hemorrhage, or both. Such changes were found in varying degree in every organ examined, although, as would be expected, not uniformly in all organs in all cases. In some patients the damage in one organ was more marked than in another. The reason for this is unknown, but such unexplained variations in degree of involvement are not unusual in other infections. However, from the evidence presented, there appears no reason for selecting one organ over another for special attention. It is true that, clinically, the collapse seen in patients with fulminating meningococcemia simulates the collapse of acute adrenal cortical insufficiency, and that in some cases of such meningococcemia there is massive but not total destruction of adrenal cortical tissue. However, the occurrence of many similar cases without massive involvement of the adrenal cortex appears to minimize the importance of those changes as the productive cause of the clinical syndrome.

There appears to be no correlation between other described changes in the cortex and the degree of circulatory collapse. It is still possible that exhaustion

of the cortical cells may be present without histologic changes being produced. It appears probable that such exhaustion takes place more readily in the presence of overwhelming infection, but at the present time there are no criteria for the recognition of such exhaustion. For these reasons the authors believe that the term "Waterhouse-Friderichsen syndrome" should be discontinued. Either the term "fulminating meningococcic infection" or "fulminating meningococcemia" appears justified. In this series, blood cultures taken either ante mortem or post mortem were positive in 11 of 16 cases. One was contaminated, and one was taken only after rather vigorous treatment had been given (case 15). The term "meningococcic meningitis" does not sufficiently separate the fulminating cases from those commonly seen, and in this series there was no evidence of meningitis at the time of death in 4 cases.

Considering the overwhelming infection and toxemia in such cases, the value of treatment is a matter of great interest. The fact that patients presenting the classical picture of overwhelming meningococcic infection and intoxication have survived following prompt recognition and vigorous therapy, impels one to advocate the use of all available therapeutic agents in adequate dosage. Sulfadiazine by mouth may be satisfactory in the ordinary case of meningococcic meningitis, with or without bacteriemia, but this drug should be used intravenously, in adequate dosage, if the greatest value is to be obtained in the fulminating type of this infection. It is quite apparent that penicillin should be used in conjunction with sulfonamide therapy and that in the cases showing evidence of meningeal involvement it should be administered intrathecally as well as parenterally in adequate and sustained dosage. The use of antimeningococcic serum has been practically discontinued in the treatment of meningococcic meningitis. It is apparent, however, that in the fulminating case the patient needs assistance in combating the overwhelming infection and toxemia. The use of antimeningococcic serum in adequate dosage is definitely indicated in the suspected presence of severe infection and intoxication. Adrenal cortical extract has been used by those who believe that the peripheral vascular collapse is due to adrenal damage. At the present time its use must be considered empiric. In this series, only 4 patients were given what appeared to be adequate treatment; four were seen too late for any effective treatment, and in the remainder there was either no recognition of the cause or treatment was inadequate. (Am. J. Pathol., July '48 - J. H. Ferguson and O. D. Chapman)

* * * * * *

Weather Conditions Affecting Dental Anesthesia: In the use of local anesthetics in operations on the teeth over a period of more than 20 years, the author observed numerous instances in which he was unable to obtain complete anesthesia of the dental pulp. In certain cases a second injection has produced the desired result, but in some even a third injection has not resulted in pulp anesthesia. A few patients have evidenced minor toxic reactions. This investigation was begun to determine the possible relationship between weather conditions and the reactions of patients to local anesthetics. Only the preliminary phases of this subject are reported.

All observations are from the author's practice of general dentistry, exclusive of surgery and orthodontia, in Beverly Hills, California. They cover the two-year period from 1 July 1945 to 30 June 1947. During this time 1,319 local anesthetics were administered for purposes of cavity preparation upon vital teeth. Multiple cavity preparations were done under many of these anesthetics. A single patient may be represented several times in the series.

Only 3 types of injection were used:

1. Mandibular block for the inferior alveolar nerve: used for all operations on the mandibular teeth.

2. Tuberosity block of the posterior division of the superior alveolar nerve: used for all operations on the posterior maxillary teeth, and occasionally adequate for the whole quadrant.

3. Subperiosteal: used for operations on the anterior maxillary teeth, and occasionally on the premolars. This injection is made very slowly to avoid trauma and possible ballooning of the tissues.

No premedication was used at any time. All injections were made by the author whose technic and rate of injection have become standardized through experience over many years. The same formula of solution was used in all cases. The age range of patients anesthetized was from 5 and 1/2 to 76 years. There were 413 male patients (31 percent), and 906 female patients (69 percent).

An anesthetic reaction has been designated toxic when the operator observed any objective symptom such as blanching, tremor, or tachycardia, or when the patient reported a subjective symptom such as slight nausea, weakness in the knees or elbows, or a feeling of fullness in the throat. In no instance did any reaction progress to the point of fainting, and the duration of such symptoms has in no instance exceeded three and one-half minutes. These reactions are not to be confused with those of psychic origin, for, in the author's office there is no discussion of the use of local anesthesia, the syringe is never seen by the patient, and frequently symptoms of numbness are the first knowledge the patient has that an anesthetic has been administered. Typical of psychic reactions are those which were sometimes observed prior to 1944, when surgery was still being done in the office. Some patients who had been anesthetized numerous times for cavity preparation with no reaction whatsoever, became faint, and even at times, nauseated from the same injection when made for purposes of extraction. More apprehension in the patients in this study would be expected from a discussion of the possibility of omitting local anesthesia for cavity preparation than from the anticipation of an injection.

An anesthetic was designated abnormal when there was incomplete anesthesia of the dental pulp, or when the duration of anesthesia was unusually short.

Many of the patients are represented in both categories (i.e., toxic or abnormal), but not at the same time except in one instance in which a toxic manifestation occurred with an incomplete anesthetic.

The reactions to anesthetics were recorded daily. At the end of each month a weather summary, supplied by the Weather Bureau of the United States Department of Commerce at Los Angeles, was used to mark the weather changes on the graph.

In a review of this two-year survey it has become the author's belief that the unusual experiences with local anesthetics are directly related to temperature change. Although a possible relationship or correlation may exist with the other weather factors, they are of secondary importance. The author recognizes the fact that these observations might be considered true for this particular geographic area alone. In other parts of the country, other factors, such as barometric pressure, might well be more important than they are in Southern California.

It has been shown that under environmental temperature changes the distribution of the blood deviates from the normal, becoming predominantly peripheral in distribution with a sudden rise in temperature, or predominantly in the splanchnic beds with a sudden drop in temperature, and that there is a relative anoxia in the tissues affected by reduced blood supply.

Theories on the action of local anesthetics upon the nerve tissue, whether the lipoid theory or the enzymatic theory of Rapp, are based upon the neutralization of the acid linkage of the procaine molecule by the buffers of the tissue.

Some years preceding this investigation it had been suggested that alkalinized solutions might overcome the incomplete anesthetics occasionally experienced. To that end freshly alkalinized solutions were used for second injections when an incomplete result was obtained. No improvement in result was noted at this time, and in several instances other anesthetics, such as Monocaine, and in other cases procaine hydrochloride with epinephrine, 1:50,000, were used. It was established clearly in the author's opinion that the solution used was not the cause of the incomplete anesthetic. For purposes of record, numerous samples from various batches of the solution used in this investigation have been tested and found to average pH 4.35 (colorimetric) with a range of from 4.1 to 4.6.

From the results of this study thus far, it appears that the anesthetic reactions noted are due to changes in the patient's organic state, caused by temperature change in the weather. The preponderance of incomplete anesthetics which occurred among the mandibular injections may be explained by the fact that the injection is made into a relatively less vascular area. With the increased distribution of the blood supply to the peripheral tissues, there would be a lessened buffering action available in the nerve tissue itself. Because the tuberosity and the subperiosteal injections are made in more vascular areas,

there would be a greater possible modification of the solutions by the blood supply in the area.

Minor toxic reactions occurred approximately equally among all 3 types of injections, and this fact makes it appear that the patient's organic state, very possibly the oxidative balance, is the factor which brings the unusual reaction.

Of the 1,319 consecutive local anesthetics administered for cavity preparation upon vital teeth, fifty-six (4 percent) gave incomplete pulp anesthesia of very short duration and occurred in association with temperature peaks, and nineteen (1.4 percent) gave minor toxic manifestations and occurred in association with temperature dips. (J. Dent. Research, April '48 - A. G. James)

* * * * * *

Abrasiveness of Dentifrices: Extracted teeth of nearly uniform size were mounted in low fusing metal base, with about two mm. of the cementum exposed to mechanical brushing by a hard bristle nylon brush, with various commercial dentifrices as well as a salt and baking soda mixture and plain water. One-hundred-thousand strokes were made in each test and the depth of the cut accurately measured by producing a shadow-graph on sensitized paper superimposed on a similar graph of the tooth prior to brushing. The resulting measurements were then used to estimate the number of years that would be required to cut half way through the cervical area of a maxillary cuspid measuring 7 mm. in thickness. These estimates ranged from over 6,000 years with tap water through 110 years with salt and soda, down to approximately 7.5 years with the most abrasive of the commercial powders. Tooth powders were generally found to be much more abrasive (7.6-17 years) than tooth pastes (27-61 years) with the exception of one brand of powder which was estimated at approximately 50 years.

While there may be some question concerning the accuracy in computing the probable damage to natural tooth structure in a given number of years using various dentifrices during brushing, certain evidence gained by the experiments appears to be indisputable. It is definitely established that dentifrices exhibit an abrasive action and cause a wearing away of the tooth substance at the cervix. The results from this study can be usefully employed to supplement and modify instructions to the patient in oral hygiene. (J. Dent. Research, April '48 - P. C. Kitchen and H. B. G. Robinson)

* * * * * *

Improvement in the Technic of Fenestration in Otosclerosis: In the surgical treatment of clinical otosclerosis, bone sand and bone splinters have always been the by-products of fenestrating the bony labyrinthine capsule with the electrically driven burr. When the final endosteal bony layer is fractured inwardly and pulverized, bone dust and bone splinters are pushed in the direction of the

perilymphatic space, with most of them coming to rest on the shredded endosteal membrane and the endolymphatic labyrinth. It has been a well recognized fact that when these bone particles are not meticulously removed from the region of the fenestra, they may stimulate and enhance the naturally existing tendency for osteogenesis to occur in the freshly cut bony walls of the fenestral rim.

It is for this reason that various methods of removing the fractured and pulverized endosteal layer of the bony capsule, which is seen resting on the shredded endosteal membrane and the endolymphatic labyrinth, are being practiced by otologists doing fenestration surgery.

However, every careful otologist practicing fenestration surgery could not help but observe that in fracturing and pulverizing the endosteal bony layer of the fenestral region, bone dust and bone splinters unavoidably fall into the perilymphatic space and frequently disappear beyond visualization and retrieval.

Attempts at removing bone splinters from the perilymphatic space often result in severance of some of the perilymphatic trabeculae and trabecular blood vessels, as a result of which blood escapes into the perilymphatic space.

The endolymphatic labyrinth can easily be injured by a bone splinter left within the perilymphatic space or torn in attempts to remove such a splinter from the perilymphatic space.

As a result of making careful observations in the performance of 414 revisions of fenestrated human ears, as well as in histologic studies of the temporal bones of experimentally fenestrated rhesus monkeys, the author is vinced that bone dust and bone splinters entering the perilymphatic space are a much more serious threat to the hope of obtaining and continuously maintaining practical serviceable hearing as a result of fenestration surgery than bone dust and bone splinters resting in the region of the fenestral rim. This is so because bony fragments lost in the perilymphatic space are often not removable, while bone particles in the region of the fenestral rim can, as a rule, be completely removed.

In view of the clinical and operating table observations made in the human subject after fenestration of the labyrinth for clinical otosclerosis and the histologic observations made in the fenestrated labyrinths of rhesus monkeys, it became obvious that just as long as the creation of the fenestra nov-ovalis involves fracturing inwardly and pulverization of the endosteal bony layer of the labyrinthine capsule some of the bone splinters and bone dust thus formed will frequently fall into the perilymphatic space and disappear.

The author has gradually developed the following new technic which he uses for fenestrating the surgical dome of the vestibule without creating bone splinters and bone dust:

Step 1. Creation of an Endosteal Bone Cupola on the Surgical Dome of the Vestibule. With an electrically driven 1 mm. dental polishing burr, the bony capsule of the surgical dome of the vestibule is gradually worn down to the endosteal bony layer, until it is thinned to a bluish gray transparency. The bony capsule is then slowly and gradually worn down both anterolateral and posterolateral to the bluish gray transparent area until a bluish gray cupola of endosteal bone is created on the surgical dome of the vestibule. The bone dust formed is constantly removed by irrigating with saline solution and suction.

Step 2. Circumferential Incision of the Base of the Bony Endosteal Cupola. In an absolutely blood-free surgical field free from bone debris, the base of the cupola is incised as follows: The anterolateral aspect of the base of the cupola is pierced with a small sharp perforating knife in the direction of the perilymphatic space. A linear incision is then carried from the perilymphatic space outward through the endosteum and endosteal bone along the entire circumference of the base of the cupola.

Step 3. Eversion and Removal of the Intact Bony Cupola to Uncap the Perilymphatic Space and Expose to View the Endolymphatic Labyrinth. With a flat spatula-tipped excavator, the anterolateral margin of the base of the endosteal bony cupola is engaged, gently lifted and everted in a direction posterolateral to the fenestra and removed intact. The endolymphatic labyrinth, without having been disturbed from its normal position, is thus exposed to view.

Step 4. Lead-Burnishing of the Bony Fenestral Rim to Prevent Osteogenesis Within the Bone-Dust-Free, Freshly Cut Bony Rim of the Fenestra. With a pure lead burnishing burr held in an especially devised steel pencil holder, the bony rim of the fenestra is hand burnished. (Arch. Otolaryng., March '48 - J. Lempert)

* * * * * *

Permanent Appointment and Rank Status of Officers of the U. S. Naval Reserve: 1. On 3 June 1948 the Secretary of the Navy for, and in the name of the President of the United States, appointed officers of the Naval Reserve to permanent grades. The relative precedence dates shown in NavPers 15793 dated 1 July 1948 are not dates of rank and are for the sole purpose of indicating relative seniority among officers of the Navy and Naval Reserve.

2. Each Naval Reserve officer listed, has, by virtue of his permanent appointment, the same grade as his contemporary in the regular Navy. The regular Navy contemporary of a Reserve officer is an officer of the regular Navy who, on 1 October 1945 had the same precedence as the Reserve officer, based on the conditions of relative seniority and active duty in existence at that time.

3. Excepted from these appointments are retired Reserve officers, Reserve officers on active duty paid from the appropriation "Pay and Subsistence" and "Transportation and Recruiting of Naval Personnel," Reserve officers who already hold permanent appointments in the same grades to which they would be appointed, and Reserve officers unable to qualify under the requirements of paragraph 5 below.

4. Commanding officers of all naval activities, Naval Reserve inspector-instructors, officers-in-charge Navy recruiting stations, and commanding officers of Organized Naval Reserve commands have been directed by the Chief of Naval Personnel to effect the appointments of qualified officers concerned, upon request.

5. Officers may appear at any naval activity to effect their appointments. No orders are required and officers will not be ordered to active duty for the sole purpose of effecting these appointments.

In order to effect his appointment, each officer is required to have in his possession, suitable identification and positive evidence that he received a Certificate of Satisfactory Service if he has been released from active duty. Officers concerned who have lost their evidence of receipt of a Certificate of Satisfactory Service should request duplicates from the Bureau of Naval Personnel.

He must also make a certified statement as to his physical condition and take the physical examination, if appropriate. Each officer reporting a material change in physical condition shall be physically examined by a board consisting of one or more medical officers and one dental officer, to determine whether or not he is physically qualified for the appointment.

In effecting his (or her) appointment, each officer will execute an Acceptance and Oath of Office for permanent appointment in the Naval Reserve (NavPers 357).

6. Public Law 305 - 79th Congress, approved 21 February 1946, provides that Naval Reserve officers, upon return to inactive status, shall have the highest grades and ranks in which, as determined by the Secretary of the Navy, they served satisfactorily under temporary appointments. Officers who have served in higher grades than those to which permanently appointed, continue to have, subsequent to their release from active duty, the higher grades indicated in NavPers 15993 of 1 July 1948 and may wear the uniform and bear the title of such higher grades, and while performing training duty or attending drills receive pay based upon such higher grades.

7. Any officer who does not desire to accept the appointment authorized, shall submit a statement to that effect to the Chief of Naval Personnel via the commandant of the appropriate naval district, stating the reasons therefor and whether or not he (or she) desires to continue in the status of an officer of the Naval Reserve. (Personnel Division, BuMed)

* * * * * *

Training in Photofluorographic Interpretation: A six-weeks course in Photofluorographic Interpretation given at the U. S. Naval Medical School, National Naval Medical Center, Bethesda, Maryland, is available to medical officers of the regular Navy and the Naval Reserve. This short course serves as a background for further training in internal medicine, diseases of the chest, and radiology.

Interested medical officers should submit an official request to the Bureau of Medicine and Surgery for consideration. No service agreement is required. Reserve medical officers are eligible for this training providing they will have at least one year of obligated service remaining upon completion of their instruction. Requests should be submitted in accordance with instructions contained in the News Letter dated 23 May 1947, page 22. (Professional Div., BuMed)

* * * * * *

Dental Reserve Officer Refresher Course Scheduled by Navy: The U. S. Naval Dental School, National Naval Medical Center, Bethesda, Maryland, has announced the following curriculum for the Reserve Dental Officer Refresher Course (News Letter of 13 August 1948) to be conducted at the Naval Dental School, 25 October to 5 November. This training duty is planned to provide an opportunity for Reserve Dental Officers who have returned to their civilian practices to obtain two weeks special training with active duty pay and allowances.

The capacity of the Naval Dental School with respect to this training duty is limited to 44. Accordingly that number has been apportioned among the continental naval districts. Requests for assignment to this training duty should be submitted to the commandant of the naval district in which the Reserve dental officer maintains his official residence.

SCHEDULE FOR NAVAL RESERVE DENTAL OFFICERS COURSE
U. S. NAVAL DENTAL SCHOOL - 25 October - 5 November 1948

1st Week

Week of: 25 Oct 48

HOUR	MONDAY 10/25	TUESDAY 10/26	WEDNESDAY 10/27	THURSDAY 10/28	FRIDAY 10/29	SATURDAY 10/30
0810 to 0855	Log in with C.O's. Secretary		- 0745 - TRIP TO: NAVAL ACADEMY			- 0830 - Full Dentures LCdr. Denen
0900 to 0945	- 0945 - Opening Address Capt. Mitchell	Full Dentures LCdr. Denen		Full Dentures LCdr. Denen	Maxillofacial Prosthesis LCdr. Towle	
1000 to 1050	Oral Pathology Capt. Moe LCdr. Moore	Partial Dentures Cdr. Oesterling		Partial Dentures Cdr. Frechette	Court Martial Procedures LCdr. Glawson	Endodontia LCdr. Nutting
1100 to 1145	Periodontia Lt. Conant	Crown & Bridge Cdr. Johnson - 1145 - Group Picture		Crown & Bridge Lt. Pfeiffer	Property & Accounting CWO Allers	Public Speaking Dr. Beauchamp
1300 to 1350	TOUR OF: MEDICAL CENTER LCdr. Moore Lt. Owens	TOUR OF: BUREAU OF STANDARDS Dental Mat'ls. Dr. Schoonover Comme. Paffenbarger Cdr. Grunewald Cdr. Ferguson	DITTO	Court Martial Procedures LCdr. Glawson	Oral Surgery Cdr. Lesney	
1400 to 1450				Collateral Duties of a Dental Officer Cdr. Frates	Oral Diagnosis Cdr. Pollard Lt. Pfeiffer	
1500 to 1550				Professional Movies from NDS Film Library	NDS Staff Conference Guest Lecture	

2nd Week

Week of: 1 Nov 48

HOUR	MONDAY 11/1	TUESDAY 11/2	WEDNESDAY 11/3	THURSDAY 11/4	FRIDAY 11/5
0810 to 0855			- 0745 - TRIP TO: QUANTICO VIRGINIA		- 0830 - Physical Examination
0900 to 0945	Dental Research Methods Cdr. Schlack	Recent Findings in Dental Research Dr. Dean, USPHS		Oral Cancer Capt. Moe LCdr. Moore	C H E C K
1000 to 1050	Atomic Warfare	Biochemistry Cdr. Trumper		Arctic and Antarctic Expeditions Lt. Owens	I N G
1100 to 1145	Capt. C. F. Behrens	Ocular Prosthesis LCdr. Towle		Biochemistry Cdr. Trumper	O U T
1300 to 1350	Property & Accounting CWO Allers	Reserved for Personal Business: BuPers Record Section Ships Service Libraries Small Stores Dent. Museums etc.	DITTO	Pharmacology Dr. Morgan	Checking Out
1400 to 1450	Anesthesia Dr. Tuohy			Oral Bacteriology LCdr. Nutting	
1500 to 1550	Operative Dentistry Cdr. Turner			Maxillofacial Surgery Cdr. Lesney	GRADUATION

NOTE: LCdr. P. A. Moore will act as School Representative in general charge of all details in connection with field trips, tours, etc., of the group.

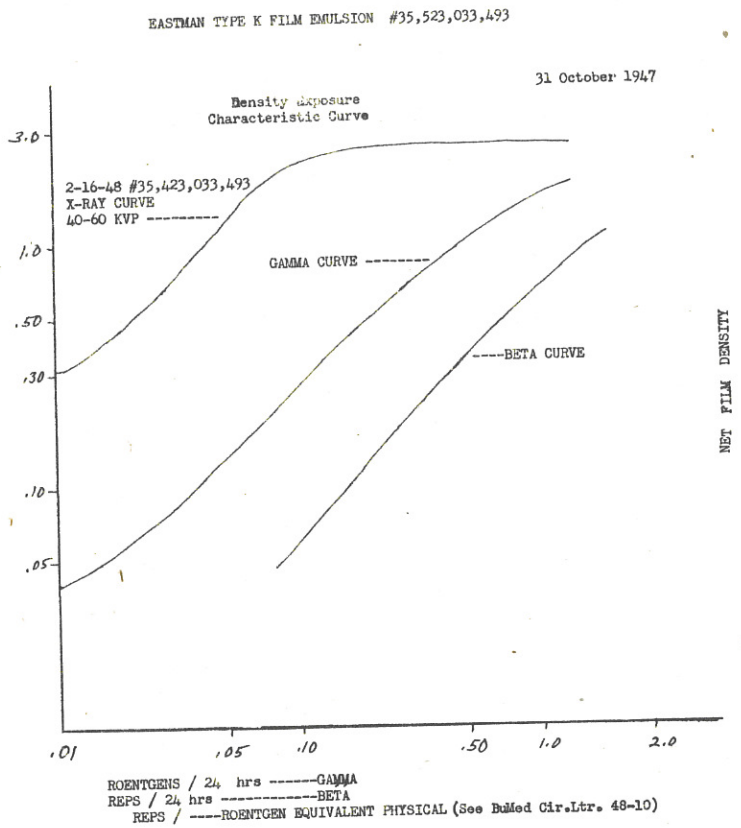
The Photodosimetry Program of the Medical Department of the Navy: In the Medical News Letter, Volume 11, Number 4, page 25, 13 February 1948, there appeared an article encouraging naval hospitals to give all possible consideration to the establishment in their departments of radiology of a program for the monitoring of personnel by means of photodosimetry. It is believed that the adoption of such a program would render personnel more safety conscious by reducing any tendency to needless exposure, and by helping to prevent exposure beyond permissible limits. The wider application of this safety practice will also afford training to personnel which will be needed for future developments.

It is planned that in the near future all naval hospitals as well as certain dispensaries and other activities will be required to establish a Photodosimetry Unit. Meanwhile all hospitals and major dispensaries are urged to do so at the earliest practicable time on a voluntary basis.

A brief description follows of the methods used in photodosimetry as presented in Radiological Defense, Volume 1, published under the auspices of the Armed Forces Special Weapons Project:

By photodosimetry is meant the determination of the extent of exposure to ionizing radiation (usually gamma, beta, and x-radiation) by measuring the degree of darkening which takes place when photographic film exposed to such radiation is developed. A photographic film packaged similarly to a dental x-ray film and called a film badge is exposed to an unknown quantity of ionizing radiation. It is developed in approximately the same way as an x-ray film and is then compared with films which have been exposed to known amounts of gamma rays or x-rays and which have been developed and processed together with the unknown films, both control and unknown films being of the same manufacturer's lot. In this manner, differences in film density due to any variation in processing technics, or to any exposure from an extraneous source can be evaluated. Control films of the same lot which have been exposed to known amounts of ionizing radiation are placed in each box or package of film prior to issue and are so marked.

The blackness of the processed film is measured with a densitometer. In this instrument light from a strong source is focused to a small point and allowed to fall on a photoelectric cell which is connected to a meter. When the light falls directly on the cell, a meter reading will be obtained which is proportional to the light intensity, I_o. When the film is put in the light path, some of the light will be absorbed by the developed silver and a lower reading corresponding to an intensity, I, will result. The readings on the meter scale are expressed as the logarithm of the ratio, $\frac{I_o}{I}$. On the sample graph on the next page which is drawn on logarithm paper, the logarithm of the density ratio, or the meter reading, is plotted against the logarithm of the degree of exposure of a film in roentgens. A similar curve is plotted for the films of each shipment from films from that shipment which have been exposed to known amounts of radiation and this curve is used in determining the degree of exposure of the films used for monitoring.



One type of emulsion can respond to only a limited range of degrees of exposure. If a different exposure range is desired, a different emulsion can be used.

Although dosimetry by photographic methods is not as accurate as that by electrical methods in the laboratory, it plays a very important role in radiological safety. A film is one of the simplest detectors of radiation. It is small and light and can be obtained with a wide range of sensitivity. It provides a permanent record of exposures and has no electronic circuit to get out of order. It can be used to monitor an area or an object as well as personnel. For many applications these factors more than outweigh the disadvantages of film processing, the time required to obtain a measurement, and the variation inherent in photographic material.

Although the foregoing is a very brief discussion of the technical aspects of photodosimetry it will serve to give some insight concerning this procedure. It is the desire of the Bureau of Medicine and Surgery that photodosimetry units be established in all naval activities where persons are repeatedly exposed to ionizing radiation. Such personnel include radiologists, x-ray technicians (both clinical and industrial), workers who are employed as dial painters, and instrument workers and others who come in contact with radioactive "self-luminous" paint, and other radioactive materials.

Trained personnel must be available to establish a photodosimetry program. Men who were trained in the X-Ray Technicians School at the Naval Medical School, National Naval Medical Center, Bethesda, Maryland, starting with the class which commenced on 29 September 1947 have had training in photodosimetry, and all men in subsequent classes will get this training. All the details of numbering, recording, issuing, logging, processing, and evaluating exposure readings of the film badges, as well as preparation of routine reports, are familiar to men so trained. Refresher training in photographic dosimetry is available at the Radiological Defense Laboratory, Naval Shipyard, San Francisco, for x-ray technicians whose training did not include photodosimetry. Requests for trained personnel or the training of personnel may be submitted through regular channels.

Supplies of film badges may be obtained upon request to the Bureau of Medicine and Surgery Projects Officer, Radiological Defense Laboratory, San Francisco Naval Shipyard. The request should state the number of badges required per month as well as the number on hand and should ordinarily be made for not more than a three months' supply. Under the present conditions it is thought that a film badge should be worn for one week. Where there are fewer than 10 people repeatedly exposed to ionizing radiation, the exposed film badges may be submitted for processing by arrangement with the nearest photodosimetry processing unit or with the Radiological Defense Laboratory , Naval Shipyard, San Francisco. Activities where more than 10 persons are so exposed should establish their own processing unit.

Because holders for use in pinning the film badge to the outer clothing are not available at present, they should be fabricated locally.

Densitometers used in photodosimetry shall be of an approved photoelectric type. At the present time they must be obtained by local purchase. Densitometers at present approved by the Bureau are:

Weston Photographic Analyzer - Model 877 (A line voltage regulator should be used with this instrument to provide a constant light source.)
Ansco-Sweet Densitometer - (Navy designation PH614/U)

The Bureau of Medicine and Surgery is to be notified when a photodosimetry program has been set up. Included in this notification will be listed the name and rank of the officer under whose supervision the unit is to function, the equipment which is on hand, and the estimated number of persons who are repeatedly exposed to ionizing radiation.

Medical officers concerned are to submit to the Bureau of Medicine and Surgery also a Monthly Photographic Dosimetry Report of all exposed personnel, indicating in columns the name, rate, occupation, number of days on duty involving exposure to ionizing radiation, total gamma or x-radiation received to date, and total beta radiation received to date, if any. In the event that any individual's badge shows that he has received any exposure in excess of an average of 0.1 r per 24 hours the circumstances connected therewith shall be explained as a part of the same report. Each month the total dosage of ionizing radiation received will be recorded in the health records of the exposed service personnel together with the amount of exposure for the preceding month. Also, a monthly roster of all personnel engaged in the processing or reading of film badges is to be submitted to the Bureau of Medicine and Surgery. A permanent log listing film badge numbers, name and rate of persons to whom the badges are issued, date of issue, and date of return of the film badges will be kept by the Photodosimetry Unit.

Further information concerning photodosimetry and radiological safety may be obtained by referring to Bureau of Medicine and Surgery Circular Letter No.

48-10, to the Manual of Radiological Safety (NavMed P-1283 Rev. March 1948), and to Radiological Defense, Volume 1 (Armed Forces Special Weapons Project).

A technical manual on photodosimetry is under preparation and will be available within the next few months. (Atomic Defense Div., BuMed)

* * * * * *

BUMED CIRCULAR LETTER 48-85 6 August 1948

To: NavHosps, NavDisps, Stations having Dispensaries, Ships (Major)

Subj: Pharmacy Reference Library

Ref: (a) BuMed CircLtr No. 48-1 dtd 2 Jan 1948.

1. The following listed books constitute a useful reference library which is considered desirable for activities providing pharmaceutical services. Procurement of nonstandard books will be made in accordance with reference (a):

(1) U. S. Pharmacopeia XIII (current edition) and Supplements

(2) National Formulary VIII (current edition) and Supplements

(3) U. S. Dispensatory, 24th edition

(4) Mercks Index, 5th edition

(5) Textbook on Pharmacy (general)

* (Practice of Pharmacy, 9th edition, Cook-Martin)
* (Principles of Pharmacy, 5th edition, Arny-Fischelis)
* (American Pharmacy, Vol. I, II, III, Lyman)

(6) Textbook on Dispensing Pharmacy

* (Dispensing Pharmacy, 1947, Husa)
* (Art of Compounding, Powers-Crossen)

(7) Textbook on Pharmaceutical Arithmetic

* (Pharmaceutical Calculations, Bradley-Gustafson)
* (Pharmaceutical and Chemical Arithmetic, Sturmer)
* (Arithmetic of Pharmacy, Stevens)

(8) Modern Drug Encyclopedia and Therapeutic Drug Guide, and Supplements, Gutman

(9) New and Non-Official Remedies 1947 (current edition)

(10) Pharmaceutical Recipe Book III

(11) Textbook on Pharmacology

* (Pharmacological Basis of Therapeutics, Goodman-Gilman)
* (Manual of Pharmacology, Sollmann)
* (Materia Medica, Pharmacology, Therapeutics, Bastedo)

(12) Medical Dictionary

*Select one.

--BuMed. C. A. Swanson

* * * * * *

BUMED CIRCULAR LETTER 48-86 9 August 1948

To: AlNav Stas and Hospital Ships

Subj: Hospitalization of Beneficiaries of the U. S. Public Health Service in Naval Medical Facilities

Refs: (a) Pars. 4147, 4148 and 4149, ManMedDept, USN
(b) Pars. 4155, 4157 and 4158, ManMedDept, USN

1. The U. S. Public Health Service has instituted a new procedure for obtaining hospitalization for its beneficiaries in the medical facilities of other Government agencies. The new procedure was designed to improve the maintenance of medical records on these patients and to expedite the processing of Vouchers for Transfers between Appropriations and/or Funds, Standard Form No. 1080, by ensuring that the PHS authorization is shown in each case, as required by the General Accounting Office. In order to comply with the new procedure, naval medical facilities shall be guided by the instructions outlined in the following paragraphs.

2. In locations where the U. S. Public Health Service has a medical relief station, quarantine station, or district office but no in-patient facilities, its beneficiaries may be referred to naval medical facilities for medical care and treatment. The beneficiary will present a Treatment Authorization, Form PHS 894(HD), signed by the referring Public Health Service medical officer and an original and 2 copies of Form PHS 484-1(HD), Clinical Record Brief, completed through item 37 except for item 7, "Date and Hour Admitted." When such a patient is admitted, the hospital should fill in item 7 on the Briefs and return the second copy to the referring office. After treatment is completed, the naval

medical facility shall complete the Briefs, forward the original to the referring office, and retain the first copy for its files. The Treatment Authorization for each patient should be submitted to this Bureau with the first monthly report which contains the name of the patient.

3. There may be occasions when a U. S. Public Health Service beneficiary will apply for admission to a naval medical facility on his own initiative, without the usual formal request and record sheets. Applicants of this kind should be admitted only in genuine emergencies when they are physically unable to go to a U. S. Public Health Service activity for authorization or the PHS office is closed. In these cases, the naval medical facility should telephone or telegraph the nearest Public Health Service station as soon as possible, giving all available information on the patient's status as a PHS beneficiary. If the patient's eligibility is clear, the PHS station will give immediate authority for treatment; if it is questionable, the PHS medical officer in charge may give provisional authority until he can check further. As soon as the patient's eligibility has been verified, the PHS office will forward to the naval medical facility, admitting the patient, a signed Treatment Authorization and 3 blank Clinical Record Briefs. The admitting medical facility shall complete the Briefs through item 37, returning the third copy to the PHS station. The procedure from this point on is the same as for patients formally referred, and which is outlined in paragraph 2 above.

4. Public Health Service medical officers in charge of PHS stations, which will utilize naval medical facilities, will get in touch with the proper naval authorities concerned to discuss the operation of the new procedure, and all additional detailed arrangements that may be required can be worked out locally, between the PHS medical officers and the proper naval authorities of each naval activity.

5. Beneficiaries of the U. S. Public Health Service are: (a) Coast Guard personnel, active duty; (b) Coast Guard personnel, retired, inactive; (c) U. S. Merchant Marine; (d) U. S. Maritime Service; and (e) U. S. Public Health Service Officers.

--BuMed. C. A. Swanson

* * * * * *

BUMED CIRCULAR LETTER 48-87 11 August 1943

To: Ships, Stations, and Other Activities having Dental Officers

Subj: Advance Change, ManMedDept (Cancellation of Annual Dental Report)

1. The Annual Dental Report is hereby canceled. Delete from the ManMedDept: Paragraphs 1382 (added by enclosure to BuMed C.L. 47-138) and 5130 and section headings relating thereto, line 12 of Paragraph 513 on page 476, and index references to this report on pages 509, 527, and 586.

2. Subject change will be included in future printed page changes as deletions.

--BuMed. C. A. Swanson

* * * * * *

BUMED CIRCULAR LETTER 48-88 13 August 1948

To: Medical Officers in Command, Naval Hospitals (Continental)

Subj: Shipment to Naval Hospitals by Tobacco or Other Companies of Donated Cigarettes Withdrawn from Tax at the Factory for the Use of the United States.

This letter (1) states that the continued acceptance of cigarettes donated and shipped to selected naval hospitals by a tobacco or other company for use by patients is approved, and (2) furnishes instructions concerning the procedures to be carried out by the addressees in connection with such gifts.

* * * * * *